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# DIAGNOSIS OF UNICYSTIC AMELOBLASTOMA USING CALRETININ - CASE REPORT

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## ABSTRACT

Ameloblastomas are the commonest occurring tumors. More than 80% of all ameloblastomas are solid or multicystic variants (SMA), in which unicystic ameloblastoma (UA) is an important clinicopathologic variety. It occupies the remaining 20% of the cases. UA clinicopathologically resembles an odontogenic cyst but with few exceptions. KCOT, characterized histologically, by a palisaded basal cell layer of basophilic columnar cells and a surface of corrugated parakeratin, sometimes with spongiosis. This resembles very closely with the stellate reticulum like cells. If the tissue sample is small and if the neoplastic epithelium displays reactive changes induced by inflammation, it can closely resemble unicystic ameloblastoma histologically. Thus, at times, both lesions become histologically indistinguishable. As Calretinin is used as a specific immunohistochemical marker for neoplastic ameloblastic epithelium.

We report a case of UA exhibiting histologically disconnected islands in the capsule without accompanied bony invasion seen in left premolar and molar region of mandible in a 38 year old female patient. The final diagnosis in this case was confirmed by using this marker. The final diagnosis of Unicystic Ameloblastoma with disconnected active intra-mural ameloblastomatous follicle was given.

**KEYWORDS:** Ameloblastoma, Unicystic Ameloblastoma, KCOT, Calretinin.

**INTRODUCTION:**
Ameloblastomas are the commonest occurring tumors. More than 80% of all ameloblastomas are solid or multicystic variants (SMA), in which unicystic ameloblastoma(UA) is an important clinicopathologic variety. It occupys the remaining 20% of the cases (Nagalaxmi et al. 2013). The concept of unicystic ameloblastoma(UA) was first introduced by Robinson and Martinez in 1977 and there were various names given such as mural, monocystic, intracystic, cystogenic, or cystic ameloblastoma (Singh et al., 2010; Eversole et al. 1984).

UA clinicopathologically resembles an odontogenic cyst but with few exceptions. The radiographic representation is commonly unilocular (especially impaction associated ones) but may be multilocular. It clinically often appears at a yonger age than SMA. Histologically, it is cystic in architecture.

Thus clinically and radiographically it often resembles of an odontogenic cyst but in histologic examination show a typical ameloblastomatous epithelium lining part of the cyst cavity, with or without luminal and/or mural tumor proliferation. Males are slightly more often affected than females (1.5:1) when UAs associated with an impacted tooth are considered. On the other hand when the tumour is impaction-associated, the ratio seems to be reversed (M: F=1:1.8) (Philipsen and Reichart, 1998).4 Irrespective to the impaction, mandible is predominantly affected over maxilla (Philipsen and Reichart, 1998).

We report a case of UA exhibiting histologically disconnected islands in the capsule without accompanied bony invasion seen in left premolar- molar region of mandible in a 38 year old female patient.

**CASE REPORT :**
A 38-year-old female patient came to the Department of Oral Medicine and Radiology of ITS Dental College, Greater Noida complaining of pain and swelling in the left lower back tooth region since 3 years. Patient was apparently well 3 years back when she started feeling mild pain and swelling intermittently. Patient had undergone the extraction of lower left first and second premolar and first molar (34, 35, 36) 6 months ago. During intraoral inspection mild smooth surfaced swelling was present in buccal and lingual vestibule irt 34 & 35 and was measuring approximately 1.5x1.5cms causing mild buccal vestibular obliterartion. The swelling was soft and tender with no rise in local temperature and few bleeding points were present. The patient did not report any systemic health problems.The extraoral examination did not reveal any abnormality.

An orthopantomographic (Fig.1) evaluation revealed multilocular radiolucency in edentulous 34 region with radio-opaque smooth sclerotic border. 33 was root canal treated and exhibited root resorption apically.

The differential diagnosis of Residual cyst, Odontogenic keratocyst, Dentigerous cyst were made. Provisional diagnosis was unicystic ameloblastoma.

Incisional biopsy specimen (Fig.2) was taken from the buccal vestibular edentulous 34-35 region and was sent to the department of Oral Pathology for histopathologic examination (Fig3-7). The histopathological sections revealed cyst with ameloblastomatous epithelial lining and stellate reticulum like superficial cells exhibiting large keratinizing squames resembling ghost cells. Although there were no distinct calcifications in it but the ghost cell –like appearance led to the provisional diagnosis of Calcifying Odontogenic Cyst. The basal lining exhibited Vicker and Gorlin positive ameloblast like cells with superficial stellate reticulum like cells with surface squamous differentiation and areas of parakeratin formation. Focal areas of juxta-epithelial hyalinization could also be observed. The capsule was highly fibro- cellular with an area exhibiting disconnected active ameloblastomatous island.

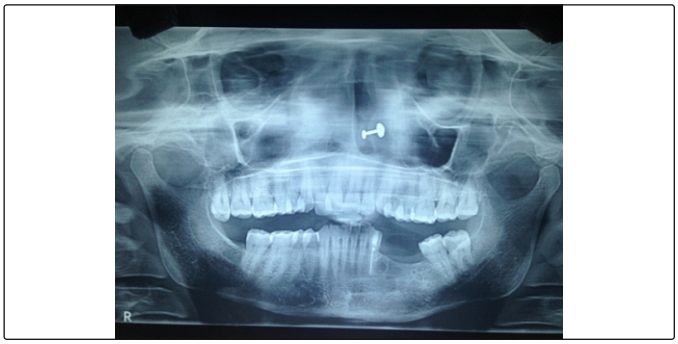

**Fig.1:** orthopantemogram exhibiting multilocular radiolucency in 33 region at the lateral border of 32

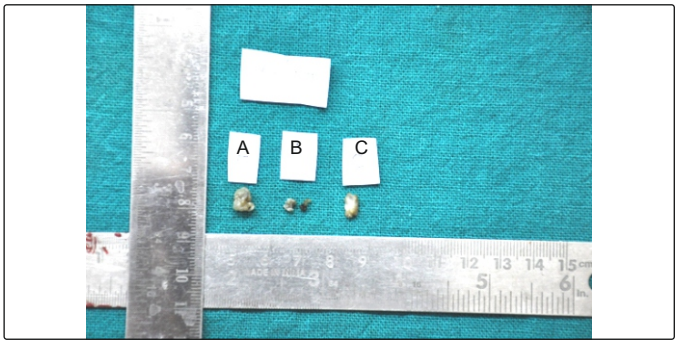


**Fig. 2:** Biopsy specimen received: **A, B:** soft tissue specimens received in 10% normal buffered formalin. It is greyish brown in color and soft in consistency. It has smooth surface and irregular borders.; **C:** hard tissue is a bit of bone which was taken for decalcification.

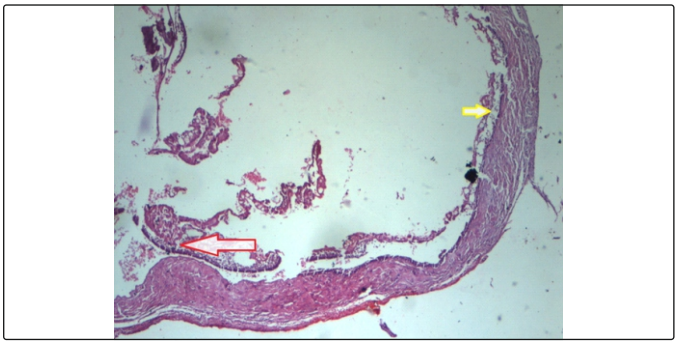

**Fig. 3:** H & E; 4x: yellow Arrow shows stellate reticulum like cells. Red Arrow shows hyperchromatic nuclei

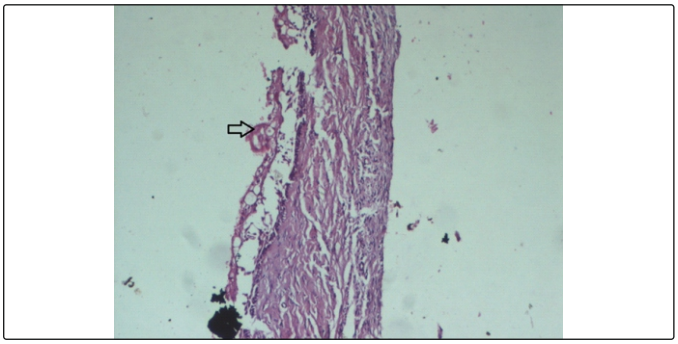

**Fig.4:** H & E;10x: Arrow shows extensive keratinization

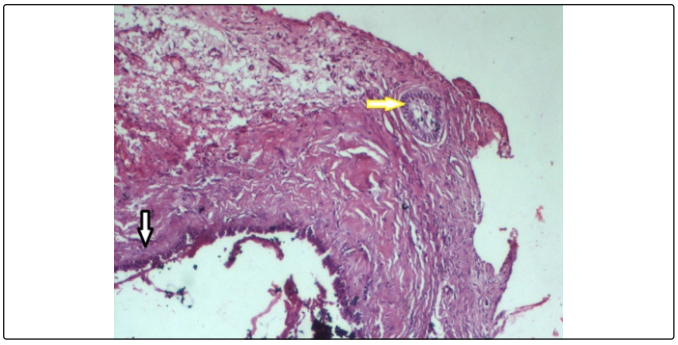

**Fig.5:** H & E;40x: yellow arrow shows disconnected ameloblastomatous island. Black arrow shows juxtaepithelial hyalanization.

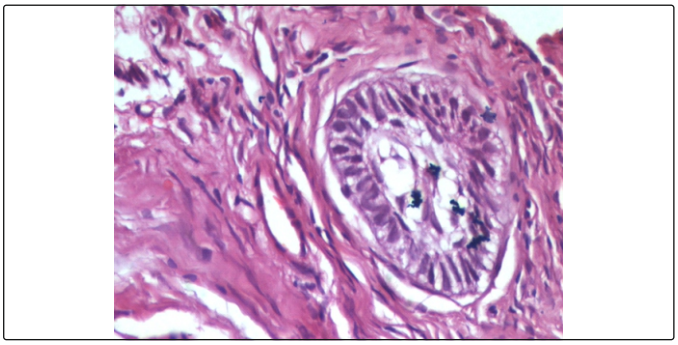

**Fig.6:** H & E; 40x: higher magnification of ameloblastomatous island

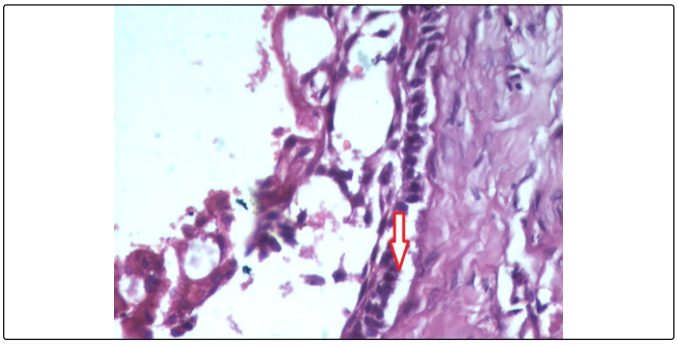

**Fig.7:** H & E; 40x: Subnucleolar vacuoles

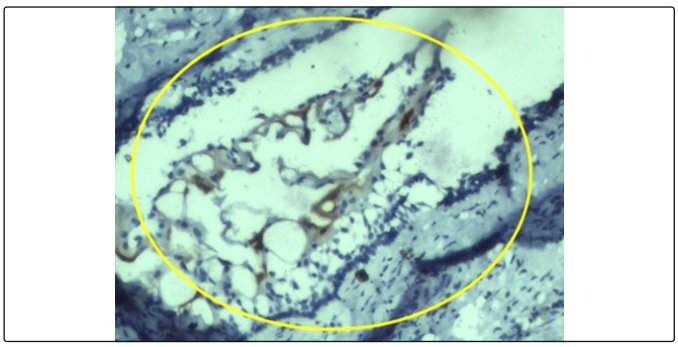

**Fig. 8:** Calretinin expression of the ameloblastic epithelium. The reactivity was observed in both the nucleus and cytoplasm of the cells.

Based on the histopathological features, diagnosis of UA with group III was made. IHC staining was performed using Calretinin in order to rule out the possibility of being any odontogenic cyst. In this case the patient is female and of 38 years and gave the history of the extracted teeth and the area of radiolucency overlaps with the diagnostic features of odontogenic keratocyst. KCOT,an aggressive cyst have a neoplastic behaviour however unicystic ameloblastoma is a neoplasm with cyst like behaviour. KCOT arises from cell rests of the dental lamina which is same as origin of ameloblastoma, and there are clinical and radiographic similarities too. Both are present as ordinary cysts in the dentulous areas. Histologically, unicystic ameloblastoma is lined in some areas but rarely entirely, by odontogenic epithelium of ameloblastoma appearance and stratified squamous epithelium in the remaining areas. The squamous metaplasia is relatively a frequent phenomenon in unicystic ameloblastoma and many of these lesions are lined by such nondescript epithelium, which can create diagnostic confusion with odontogenic cysts.

KCOT, characterized histologically, by a palisaded basal cell layer of basophilic columnar cells and a surface of corrugated parakeratin, sometimes with spongiosis. This resembles very closely with the stellate reticulum like cells. If the tissue sample is small and if the neoplastic epithelium displays reactive changes induced by inflammation, it can closely resemble unicystic ameloblastoma histologically. Thus, at times, both lesions become histologically indistinguishable.

Calretinin is a 29 kDa calcium-binding protein of the EF-hand family. It is expressed in a wide array of normal and tumorigenic tissues. Its expression in odontogenic epithelium during odontogenesis and in neoplastic odontogenic tissues has been demonstrated (Imran et al., 2016). Unicystic ameloblastoma pretence a diagnostic challenge, as its histologic presentation can be sometimes mistaken for keratocystic odontogenic tumor (KCOT) (Anandani et al., 2014). The expression of Calretinin was seen in the epithelium-derived tissues during odontogenesis in rat molar tooth germs, in neural element of tooth pulp, periodontal ligament and viscerosensory nerve fibers of oral tissues suggesting that this protein may play a part in enamel formation (Anandani et al., 2014). The results for IHC showed Calretinin expression of the ameloblastic epithelium. The reactivity was observed in both the nucleus and cytoplasm of the cells (Fig.8). As Calretinin is used as a specific immunohistochemical marker for neoplastic ameloblastic epithelium, the diagnosis of Unicystic Ameloblastoma was confirmed. The final diagnosis of Unicystic Ameloblastoma with disconnected active intra-mural ameloblastomatous follicle was given.

**DISCUSSION:**

Ameloblastoma is a benign, locally aggressive odontogenic neoplasm with variable clinical expression and accounts for 1% of all cysts/tumors of jaws and 18% of all odontogenic neoplasms (Nagalaxmi et al., 2013; Ramesh et al., 2010; Kumar et al., 2012). Unilocular ameloblastoma (UA) is a rare type of ameloblastoma, accounting for about 6% of ameloblastomas (Nagalaxmi et al., 2013; Ramesh et al., 2010; Kumar et al., 2012). It is slow growing, locally aggressive pathology and rarely metastasizes. It has a high rate of recurrence (55–90%) if not removed adequately (Nagalaxmi et al., 2013).

The pathogenesis of UA remains ambiguous. Some investigators believe that UAs arise from pre- existing odontogenic cysts, while others maintain that they arise de novo. Leider et al has proposed three pathogenic mechanisms for its evolution (Philipsen and Reichart, 1998):

(1) The reduced enamel epithelium associated with a developing tooth undergoes ameloblastic transformation with subsequent cystic development,

(2) Ameloblastomas may arise in a dentigerous or other type of dental cyst in which the neoplastic ameloblastic epithelium is preceded temporarily by a non neoplastic stratified squamous epithelial lining,

(3) A solid ameloblastoma undergoes cystic degeneration of ameloblastic islands with subsequent fusion of multiple micro cysts to develop a unicystic lesion.

Calretinin have emerged to be a specific immunohistochemical marker for neoplastic ameloblastic epithelium. Here, we made our final diagnosis using calretinin as it does not express in radicular, dentigerous, OKC and Calcifying odontogenic cyst. This helped us in completing the diagnosis as UA.

Ameloblastoma is classified based on differences in biologic behavior, treatment plan and recurrence rate as follows (Reichart and Philipsen, 2004):

(1) Classic solid/multicystic ameloblastoma,

(2) Unicystic ameloblastoma,

(3) Peripheral ameloblastoma,

(4) Desmoplastic ameloblastoma, including the so-called hybrid lesions.

It commonly occurs at a younger age group of 16–20 years, with about 50% of the cases occurring in the second decade of life (Nagalaxmi et al., 2013; Kumar et al., 2012) . The gender distribution shows a slight male predilection with a male to female ratio of 1.6 : 1. However,when the tumor is not associated with an unerupted tooth, the gender ratio is reversed to a male to female ratio of 1 : 1.8 (Kumar et al., 2012). It has been frequently observed that 90% of the cases are located in the mandible in the posterior region, followed by the parasymphysis region, the anterior maxilla, and the posteriormaxilla (Kumar et al., 2012). Patients complains of swelling and pain being an occasional presenting symptom. Small lesions are however diagnosed during routine radiographic checkup
.
In a clinicopathologic study of 57 cases of unicystic ameloblastoma, Ackermann classified UA into3 histologic groups (Reichart and Philipsen, 2004):

*Group I:* Luminal UA (tumor confined to the luminal surface of the cyst)

*Group II:* Intraluminal/plexiform UA (nodular proliferation into the lumen without infiltration of tumor cells into the connective tissue wall), and

*Group III:* Mural UA (invasive islands of ameloblastomatous epithelium in the connective tissue wall not involving the entire epithelium).

Another histologic subgrouping by Philipsen and Reichart has also been described (Nagalaxmi et al., 2013):

*Subgroup 1:* Luminal UA

*Subgroup 1.2:* Luminal and intraluminal

*Subgroup 1.2.3:* Luminal, intraluminal and intramural

*Subgroup 1.3:* Luminal and intramural

The only way to perfectly diagnose unicystic ameloblastoma is by histological examination of the entire lesion and cannot be envisaged preoperatively. The histologic criteria in the diagnosis of unicystic ameloblastoma described by Vickers and Gorlin includes (Radhika et al., 2011):

1. A cyst lined by ameloblastic epithelium with a tall columnar basal layer
2. Subnuclear vacuoles
3. Reverse polarity of hyperchromatic nucleus
4. A thin layer of edematous, degenerating stellate reticulum like cells on the surface.

Our case satisfy all the above criteria and fall into the category of Group III according to Ackermann's classification.

The UAs diagnosed as subgroups 1 and 1.2 can be treated conservatively (careful enucleation), whereas subgroups 1.2.3 and 1.3 showing intramural growths are treated via radical resection, as for a solid or multicystic ameloblastoma (Anandani et al., 2014). Recurrence rates for UA after conservative surgical treatment (curettage or enucleation) are reported to be less than 25% and a as low as 10.7% has been disclosed for UA of the intraluminal, plexiform type (Philipsen and Reichart, 1998).

**CONCLUSION:**

The diagnosis of unicystic ameloblastoma in this case was based on clinical, radiological, histopathologic, and Computed tomographic features. As it falls in the type III category Ackermann's classification, it has stong tendency of recurrence. Therefore this variant of ameloblastoma with aggressive histologic behaviour was completely resected to avoid any future recurrence. The patient is advised to follow up at regular intervals to check for any recurrences.

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